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PSORALEN-SUNLIGHT (PUVASOL) VS NARROW-BAND UVB PHOTO THERAPY IN TREATMENT OF VITILIGO: EVIDENCE BASED PROSPECTS FOR FUTURE

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Abstract:

Background: The combination of treatment with psoralen followed by sun exposure (PUVASOL) is a well-established treatment for vitiligo, but it has many disadvantages. In the past decade, there have been reports of good efficacy using narrow band UV-B therapy. Narrow-band ultraviolet B (NBUVB) is an emerging, effective and safe treatment alternative for vitiligo.

Aims: To compare the efficacy of oral PUVASOL therapy with narrow band Ultraviolet-B (NB-UVB) therapy in the treatment of vitiligo.

Settings and Design: Prospective comparative analysis was performed on 64 Patients presenting to the Skin and VD Department of Nalanda Medical College & Hospital, Patna and diagnosed as a case of vitiligo.

Methods and Materials: Patients were divided in two groups. 32 patients in each group were treated with PUVASOL and NB UVB therapy thrice weekly. 54 patients (26 in group A and 28 in group B) completed the treatment for 6 months. Results about the repigmentation, color match, adverse effects and stability were compared in both treatment groups.

Statistical analysis used: Analysis was performed using Statistical Package for Social Sciences software (version 16; SPSS). Comparisons of the 2 treatment groups were made using the exact $\chi 2$ test and statistical significance was assumed at $P<0.05$.

Results: 19 (67.85%) of 28 patients in the NB-UVB treated group showed more than 50% repigmentation compared with 10 (38.46%) of 26 in PUVASOL treated group ($p< 0.05$). Colour match of the treated area to the surrounding normal skin was found better in NBUVB-treated patients 25(89.28%) as compared to the PUVASOL group 10(38.46%). After 6 months of stopping treatment stability of repigmentation with surrounding skin was almost equal in both the groups.

Conclusion: We showed that NBUVB showed better therapeutic effects in inducing repigmentation and color match than PUVASOL therapy and lacks psoralen and sunlight related side effects. Therefore, it could be used as one of the first line medications in the treatment of vitiligo.

Key words: PUVASOL, NBUVB, Repigmentation, Color Match, Vitiligo

Introduction

Vitiligo is a primeval skin disorder that creates an immense psychosocial and cosmetic concern to the patients and their family members. Vitiligo affects all races of the world. The prevalence ranges from 0.5% to 2% worldwide.[1] The highest incidence has been recorded in India and Mexico. The incidence in India is around 3%-4%.[2] Both sexes are equally affected, and the maximum incidence is between ages 10-30 years.[3]

Conventional therapies for vitiligo require months to years of treatment and sometimes result in disappointing outcomes, particularly in difficult areas in the extremities.[4] Psoralen and UVA irradiation (PUVA) treatment has been the only successful treatment for decades. Psoralen phototherapy (psoralen + ultraviolet A, PUVA) is the mainstay of therapy in vitiligo, however its adverse effects like nausea, phototoxic reactions, risk of cataract as well as long-term carcinogenic risk limit its use. In order to avoid these inevitable complications, narrow-band ultraviolet B (NB-UVB) has been introduced recently as a probable safe and effective modality in the treatment of vitiligo.[5] The treatment is safe in children, pregnant women and lactating mothers, and has minimal adverse effects (xerosis, pruritus, skin aging, and tanning). The risk of skin cancer is minimal even with multiple treatments although there is a greater risk of phototoxicity with depigmented skin.[4]

The present study was designed to assess the improvement of patients of vitiligo treated either with PUVASOL (psoralen followed by sun exposure) or NBUVB therapy. We compared these in terms of efficacy, time to re-pigment, stability of re-pigmentation and adverse effects to determine which method is better in the treatment of vitiligo.

Methods

The present study was a comparative follow up analysis of 64 patients of vitiligo those were treated in Skin and VD Department of Nalanda Medical College & Hospital, Patna, Bihar. Patients having more than 14 years age and 25-50% of body surface involvement were included in the study (Table 1). Patients who had taken treatment for vitiligo within the last 2 months before starting treatment or those who had history of photosensitivity and any dermatoses affected by UV light were excluded. Pregnant and lactating women, patients with renal or hepatic disease, or those with immunosuppression or concomitant use of immunosuppressive medication were also excluded from the study.

Informed consent was taken from each patient. Patients were fully explained about the nature of disease and its course in addition to the method of treatment course, duration and complication of therapy and duration of follow up. After obtaining the detailed history and physical examination, a photograph of the lesions was taken. Ethical clearance was taken prior to initiation of study from college ethical committee.

Patients were divided into two groups by using random number table. No blinding was done as the same was not feasible among all patients.

Group A: Includes 32 cases with clinical diagnosis of vitiligo and on oral PUVASOL therapy. The therapy was given three times a week on non consecutive days. Oral 8-methoxypsoralen at a dose of 0.6 mg/kg was taken 2 h before sun exposure. Patients were advised to expose the vitiligenous area to measured periods of natural sunlight, starting with an initial exposure of 5 minutes and gradually increasing 5 min per week until developing slight erythema or to a maximum of 20 minutes (both sides).

Group B: Includes 32 cases with clinical diagnosis of vitiligo and on narrow band UVB therapy, which was given three times a week on nonconsecutive days. NB-UVB therapy was given using a Waldmann W UV 100 L phototherapy machine containing NB-UVB (Philips TL01) tubes. Photo testing was not done but a standard initial dose of 0.25j/cm^2 was used for all patients. An increment of 0.1 j/cm^2 in each week was done up to a maximum of 3 j/cm^2 or until faint pink erythema was achieved. Manufacturer's instructions were followed during the therapy. In case of mild erythema, the irradiation dose was held constant for subsequent treatments or until resolution of symptoms. The goal of therapy is to achieve persistent asymptomatic erythema.

Eyes were protected by UV-blocking goggles during the treatment. Genitals of the patients were kept shielded by clothes from narrowband UVB exposure. Patients were advised to use sunscreens following therapy.

Assessment of Re-pigmentation

All the patients were reviewed for re-pigmentation at the end of every month for first three months, and then assessed again at 6th month. After completion of treatment for six months patients were followed up for assessment of relapse at 9th and 12th month.

Assessment criteria

Re-pigmentation of vitiligenous areas was graded as:
Grade 0- No pigmentation
Grade1- Minimum re-pigmentation: 1-25%
Grade2- Mild re-pigmentation: 26-50%
Grade3- Moderate re-pigmentation: 51-75%
Grade 4- Excellent re-pigmentation: 76-100%

The color of re-pigmented area was compared with that of the patient's unaffected skin and the matching was compared in both groups.

Clinical evaluation was supplemented by pre and post treatment photographs of the patients under study.

Termination of therapy and follow-up

Treatment was terminated in the event of any of the following:

1. Complete or almost complete resolution of vitiligo,
2. Absence of improvement after 32 treatments or very slow progress or deterioration thereafter,
3. Intolerance of therapy necessitating termination, completion of 200 treatments in a patient's lifetime, or
4. Request by the patient for termination because of logistical reasons unrelated to the efficacy of treatment or adverse effects.

After termination of treatment because of any of these reasons, patients were assessed every 3 months for 6 months.

Statistical analysis

In group-A six patients and from group-B four patients were not compliant or not completed the therapy, hence excluded from the analysis. Analysis was performed using Statistical Package for Social Sciences software (version 16; SPSS). Demographic profiles of both the groups were statistically analyzed by using chi square ($\chi 2$) test. Comparisons of the two treatment groups were made using the unpaired t test and statistical significance was assumed at $P<0.05$.

Results

Tables

Table-1 Demographic profile of the patients

Variable		Group-A (n=32)	Group-B (n=32)	p-value
Age	15-24 years	10 (31.25%)	13 (40.62%)	0.64
	25-34 years	5 (15.62%)	3 (10.71%)	
	35-44 years	10 (31.25%)	7 (21.87%)	
	>44 years	7 (21.87%)	9 (28.12%)	
Sex	Male	14 (43.75%)	11 (34.37%)	0.44
	Female	18 (56.25%)	21 (65.62%)	
Duration of Illness	< 1 year	05 (15.62%)	07 (21.87%)	0.59
	1-3 years	21 (65.62%)	17 (53.12%)	
	>3 years	06(18.75%)	08 (25%)	
Body Area Involved	Face & Neck	17 (53.12%)	15 (46.87%)	0.98
	Upper extremity	05 (15.62%)	06 (18.75%)	
	Lower extremity	04 (12.50%)	04 (12.50%)	
	Trunk	06 (18.75%)	07 (21.87%)	
Positive Family history		15 (46.88%)	11 (34.38%)	0.43

Table: 2 Outcome of treatment over follow up

	Group A, no. (%)	Group B, no. (%)	p-value
Repigmentation at 1stmonth			
None (00)	4 (15)	0 (0)	0.02
Minimum (1-25%)	11 (42)	10 (36)	
Mild (26-50%)	7 (27)	9 (32)	
Moderate (51-75%)	4 (15)	7 (25%)	
Excellent (76-100%)	0 (0)	2 (7)	
Mean area of Re-pigmentation (%)	14.42	25.89	0.05
Repigmentation at 3rd month			
None (00)	2 (8)	0 (0)	0.01
Minimum (1-25%)	9 (35)	6 (21)	
Mild (26-50%)	8 (31)	9 (32)	
Moderate (51-75%)	7 (27)	8 (29)	
Excellent (76-100%)	0 (0)	5 (18)	
Mean area of Re-pigmentation (%)	21.15	35.71	0.02
Repigmentation at 6th month			
None (00)	0 (0)	0 (0)	0.02
Minimum (1-25%)	7 (27)	2 (7)	
Mild (26-50%)	9 (35)	7 (25)	
Moderate (51-75%)	4 (15)	8 (29)	
Excellent (76-100%)	6 (23)	11 (39)	
Mean area of Re-pigmentation (%)	33.65	50	0.02

Total 64 patients were enrolled in the study. 10 patients (6 in group A and 4 in group B) did not complete the therapy (drop outs). In this study there was female preponderance as 18(56.25%) were female in group-A and 21(65.62%) were female in group-B. Most of the patients in our study 48 patients (75%) were in the age group of 15-44 years.

Majority of cases had face & neck involvement (53.12% in group-A and 46.87% in group-B), followed by trunk (18.75% in group-A and 21.87% in group-B) then upper extremities (15.62% in group-A and 18.75% in group-B) and least cases were of lower extremities involvement (12.50% in both group-A and group-B).

Re-pigmentation was better in group-B (narrow band UVB) than group-A (PUVASOL) after 6 months of treatment. A clinical response of >50% repigmentation was seen in 67.85% in the NB-UVB group compared to 38.46% in the PUVASOL treated group. Mean improvement in Body Surface Area-Vitiligo (BSA-V) was 46.2% in group A and 62.5% in group-B at the end of 6 months of treatment (Table 2) (Figure 1-10).

Color match of the treated area to the surrounding normal skin was found better in NBUVB-treated patients 25(89.28%) as compared to the PUVASOL group 10(38.46%).

Maximum patients in our study i.e. 23 (82.14%) in group-B & 22(84.61%) in group-A complained of erythema which indicates that the regimens were almost equally erythemogenic. Only few side effects in the form of skin burning 02 (7.14%) patients in group-B and 01(3.84%) % in group-A were seen. In group-A 3 (11.53%) patients showed blister formation while in group-B no blister formation was seen. Pruritus was complained by 02(7.1%) patients in group-B and 03 (11.53%) patients in group-A. In PUVA treated group 04 (15.38%) patients developed nausea while no patients in NB-UVB group developed nausea. At the end of 3 months after treatment, no patient in either of the groups showed depigmentation of re-pigmented area while after the next 3 months, depigmentation was seen in 02 patients (7.69%) of group-A and 02 patients (7.14%) of group-B.

Discussion

The clinical experience with narrow-band UVB in vitiligo is limited. In our knowledge, no comparative trial of PUVASOL and narrow-band UVB therapy in the treatment of vitiligo has been reported yet. Re-pigmentation of the affected skin can be achieved by both the therapies. After the completion of 6 months of therapy, more than 50% improvement in BSA-V was reported to be 68% and 38% in NB-UVB and PUVASOL treated group respectively and this difference was statistically significant (p value< 0.05). First time in 1997 Westerhof *et al* reported re-pigmentation in 67% patients of NBUVB group compared with 46% in PUVA group.[7] In a meta-analysis of non-surgical therapies in generalized vitiligo by Njoo *et al*. 1998 higher success rates were observed with narrow-band UVB (63%) than oral PUVA (51%).[8] Similarly Parsad *et al.* in 2006 reported marked to complete re-pigmentation in 23.6% patients and moderate improvement in 36.8% patients among PUVA treated group, whereas in NBUVB-treated group, 41.9% patients showed marked to complete repigmentation and 32.2% showed moderate improvement.[6] Our study was concordant with the observation of Yones SS *et al* 2007 in which >50% re-pigmentation was observed in 64% of the patients in NB-UVB treated group compared with 36% in PUVA treated group.[9]

Color match of the treated area to the surrounding normal skin was found better in NBUVB-treated patients 25(89.28%) as compared to the PUVASOL group 10(38.46%), which was statistically significant. *Parsad et al* 2006 reported similar color match to surrounding skin in both NB-UVB (86%) and PUVA (35%) treatment group.[6] Yones SS et al. 2007 found excellent color match in all patients (100%) and 44% patients in NBUVB and PUVA treated group respectively (P<.001).[9]

In our study maximum patients 22(84.61%) in group-A & 23 (82.14%) in group-B complained of erythema which indicates that the regimens were equally erythemogenic. This was consistent with Parsad *et al 2006* in which 79% patients in PUVA and 72% patients in NBUVB developed grade 1 erythema.[6]

In our study, stability of repigmentation with surrounding skin was observed up to 6 months and found almost equal in both the groups but in a retrospective analysis stability of repigmentation after 12 months was significantly better in NB-UVB treated group (78.5%) compared to PUVA treated group (60%).[6] Previously in a study of PUVA therapy for vitiligo it was found that relapse usually occurs within a year of treatment.[10]

Conclusion

PUVASOL therapy is the popular mode of treatment of vitiligo in our part of country because of non availability of UV-A lamps. A major disadvantage of solar irradiation as a light source is the difficulty in quantifying UV light. The total amount of UVA reaching the skin at any one time varies widely depending on the season, time of the day, latitude and conditions of the atmosphere. Other disadvantages are lack of privacy, difficulty in monitoring the dose of ultraviolet rays and in addition to ultraviolet-A, ultraviolet B, infrared rays and visible light which are not needed for PUVA therapy may lead to undesirable effects. Our study showed that NBUVB is more effective in achieving repigmentation than PUVASOL and it is also well tolerated. NB-UVB showed better color match in comparison to PUVASOL therapy. It lacks psoralen and sunlight related side effects. Our results affirm that NB-UVB is a superior choice than PUVASOL therapy.

Figure -1 –PUVASOL therapy- Before Treatment

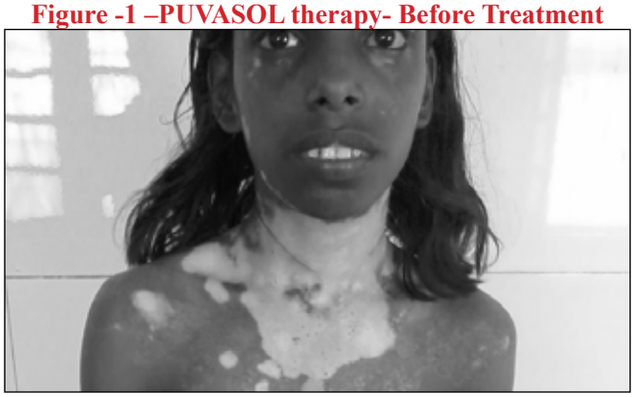


Figure – 2 –PUVASOL therapy- 6 months after treatment

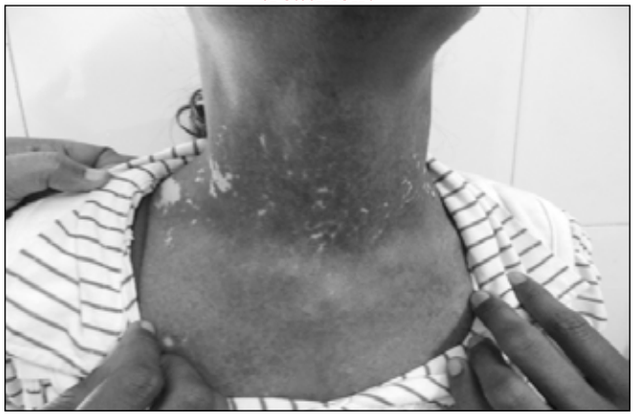


Figure -3 – PUVASOL therapy - Before treatment

Figure – 4 –PUVASOL therapy - 6 months after treatment

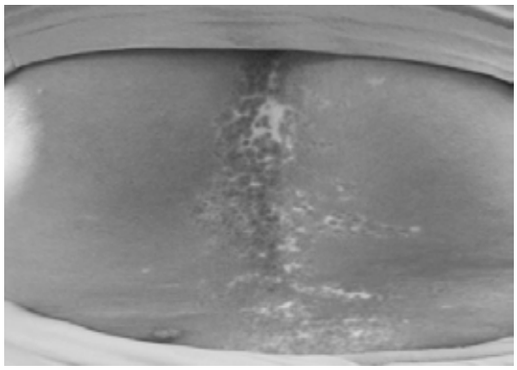


Figure –5 - NB-UVB therapy - Before treatment

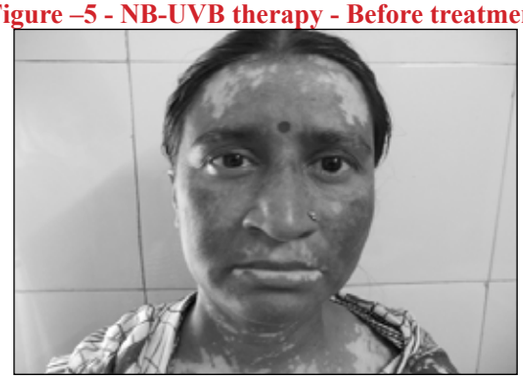


Figure –6 - NB-UVB therapy - 6 months after treatment

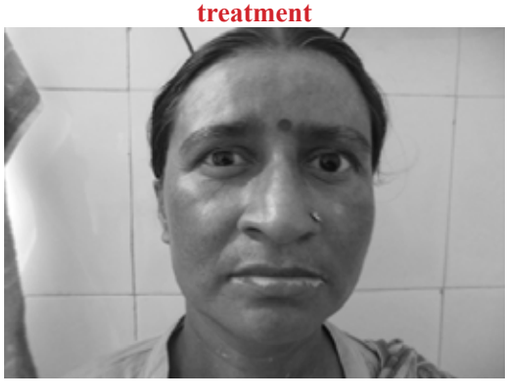


Figure – 7 - NB-UVB therapy - Before therapy

Figure -8 - NB-UVB therapy - 6 months after therapy

Figure -9 - NB-UVB therapy - Before therapy

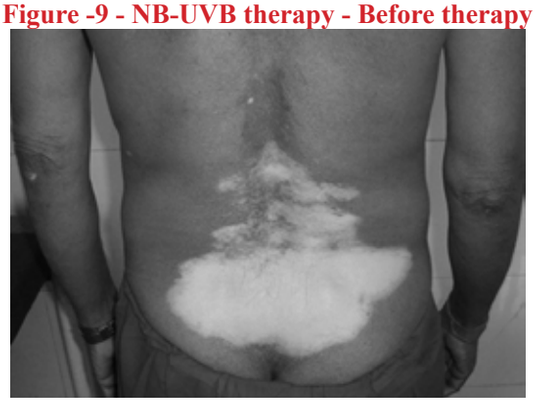
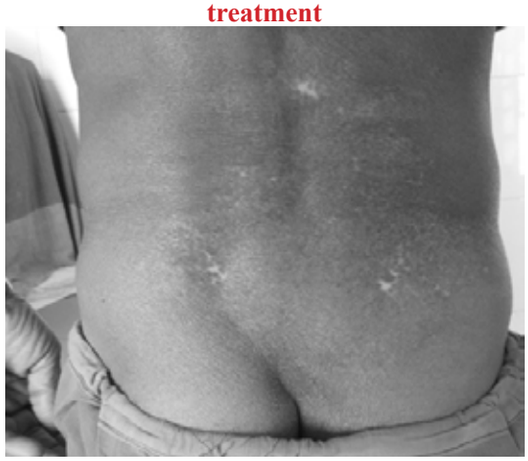


Figure – 10 - NB-UVB therapy - 6 months after treatment



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